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10/053,929

01/22/2002

Julie Straub

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05/17/2006

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EXAMINER

FUBARA, BLESSING M

ART UNIT

PAPER NUMBER

1618

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/053,929

Applicant(s)

STRAUB ET AL.

Examiner

Blessing M. Fubara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 16-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

Examiner acknowledges receipt of remarks, request for reconsideration, and rule 131 terminal disclaimer, all filed 3/8/06. Claims 16-21 are pending.

#### ***Priority***

Examiner acknowledges applicants' claim of this application as a continuation-in-part of application serial number 09/433,486 filed 11/04/1999. However, the 0.5 m<sup>2</sup>/ml, which is recited in claim 16, is not supported by application 09/433,486, now US 6,395,300 B1. There is support for particles having surface area greater than 0.9 m<sup>2</sup>/ml. Therefore, this application cannot enjoy the benefit of the filing date of the US 6,395,300 and the priority claim of the 6,395,300.

Furthermore, on page 3 of the remarks, applicants state that the filing date of the examined application is Nov. 3, 2000; but the filing date of the examined application is 1/22/2002.

#### **Response to the Rule 131 Declaration:**

Receipt is acknowledged of the rule 131 declarations. However, the pages of exhibit A is not legible and this Office action is made non-final, rejection repeated, to afford applicants the opportunity to provide legible copies of the notebook in exhibit A.

#### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (US 2001/0018072).

Unger discloses solid porous matrix that contains bioactive agent, surfactant and solvent (abstract) and a bicarbonate (paragraph 167); the solvent can be organic or aqueous (paragraph 74); the drying methods include, lyophilizing, spray drying, and the combination thereof (paragraphs 14 and 76); some of the bioactive agents that can be prepared according to Unger are anti-neoplastic agents, methotrexate, adriamycin (paragraph 135). Surfactant is an excipient. Ammonium carbonate is a volatile pore forming salt. The instant method comprises steps a-d and the steps a-c read on mixing the bioactive agent, the volatile pore forming agent and excipient and removes the solvent by lyophilizing or spray drying. Unger does not specifically disclose the claimed method steps. However, there is no demonstration that the recited method steps provides unexpected results to the porous matrix and also that the specific method steps are known in the art for the production of powder formulation (for example, column 2, lines 49-51; column 3, line 30 and column 9, line 41, of US 5,976,574 issued to Gordon, Nov. 02, 1999 a teaching reference discloses preparing powder by dissolving a drug in the solvent, adding excipient to the solution and then spray drying). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a porous matrix according to Unger. One having ordinary skill in the art would have been motivated to use the known steps of preparing the powder with the expectation of forming a porous matrix. In the absence of showing factual evidence, the recited steps of making the porous matrix does not patentably distinguish the claimed invention over the prior art.

***Response to Arguments***

Applicants argue that Unger does not use a volatile solid pore-forming agent since the blowing agent is methylene chloride, which is a liquid and that Unger does not dissolve the therapeutic agent in the solvent.

3. Applicants' arguments filed 01/04/05 have been fully considered but they are not persuasive.

While Unger discloses incorporating methylene chloride as a blowing agent, Unger discloses the presence of ammonium bicarbonate which upon spray drying would be removed and ammonium bicarbonate is one of the volatile solid pore-forming agents recited in claim 17. The comprising language of the claim is open. Unger discloses using organic solvent as discussed above.

Regarding Gordon, it is respectfully noted to the applicants that examiner was attempting to respond to applicants' argument on the Gordon art to present the fact that Gordon does indeed disclose porous nature of the powder but agrees with applicants that Gordon does not disclose volatile **solid** pore forming agent.

4. Claims 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tarara et al. (US 6,565,885).

Tarara discloses method of preparing perforated microstructure powder formulation (abstract; column 3, lines 42-48, 66, 67; column 4, lines 1-19); the perforated microstructure powder have bulk density of 0.5 g/cm<sup>3</sup> (column 4, lines 20-24); the microstructure powder contains surfactant, excipients bioactive agent, synthetic or natural polymers, rigidifying excipients and ammonium carbonate, ammonium acetate, ammonium chloride and camphor are

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amongst are few of the salts contemplated for use as rigidifying excipients (column 4, lines 25-46; column 7, lines 8-14; column 11, line 64 to column 12 line 49); the bioactive agents formulated as the powder formulation are listed in column 6, lines 39-52, column line 1 to column 14 line 47; the process involves preparing a feed solution that contains active agent, blowing agent (column 5, line 5 to column 6 line 35) water and volatile solvents (column 22, lines 32 and 33), ammonium carbonate and camphor, rigidifying excipients (column 16, lines 30-35); processes for drying the feed solution include spray drying, vacuum drying, solvent extraction, emulsification or lyophilization, and combinations thereof (column 5, lines 9, 36; column 15, lines 9-22, 26-67). In another embodiment, the perforated microstructure can be prepared by a double emulsion method where the medicament is first dispersed in a polymer dissolved in organic solvent such as methylene chloride (column 22, lines 40-44). The tap density of the highly porous powder in Tarara is less than  $0.1 \text{ g/cm}^3$  ( $0.1 \text{ g/mL}$ ) in Examples X-X111.

Although Tarara identifies fluorinated compounds and non-fluorinated oils as blowing agent, the feed solution contains volatile organic compounds such as ammonium carbonate, ammonium acetate, ammonium chloride and camphor are included in the feed solution and lyophilization, vacuum drying or spray drying would remove these compounds and further provide voids in the structure; and also, Tarara specifically discloses the feed solution can also contain compounds that can sublime upon spray drying (column 16, lines 27-33). Ammonium carbonate, ammonium acetate, ammonium chloride and camphor are volatile solids. The polymer and surfactants are excipients. One of the objects of Tarara is stabilized preparation that is suitable for pulmonary administration and the particles of Tarara resist aggregation

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(column 3, lines 17-33). Although Tarara does not specifically state the amount of active agent present in the powder formulation, it is within the purview of the skilled artisan or the person of ordinary skill to determine the amount of active agent desired in the powder formulation. When the amount of methanol and hot water are excluded since evaporation would remove the volatiles, water removable by vacuum drying or spray drying, the percent amount of the beclomethasone dipropionate (BDP) in example XI is approximately 13%, which lies within broadly claimed 1-95% of drug in claim 19.

Tarara discloses the process of the claimed invention. Changes in the order of performing the process steps is prima facie obvious in the absence of new and unexpected results and selection of any order of mixing the active agent, solvent, pore forming agent and excipient is prima facie obvious, *In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930); *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946). The claimed tap density of the porous powder is less than or equal to 1.0 g/ml. The tap density of the disclosed powder is less than 0.1 g/mL. However, there is no demonstration that the claimed tap density of  $\leq 1.0$  g/ml provides unusual results. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention to prepare the porous microstructure powder according to the process of Tarara. One having ordinary skill in the art would have been motivated to use the process of Tarara with the expectation of producing porous microstructure and in the absence of factual evidence, the claimed tap density does not distinguish the claimed process over the disclosed process. Both processes lead to porous structures.

Response to the rule 131 declaration:

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Applicants attempted to antedate the examined claims to September 29, 1997. However, the data presented is not legible. The rejection is maintained pending receipt of legible copy of the Exhibit A, current Office action is made non-final and a request is made to applicants to provide legible copy of exhibit A

5. Claims 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathiowitz et al. (US 5,271,961) or Khan et al. (US 5,413,797).

Mathiowitz: Mathiowitz discloses preparation of porous microspheres via vacuum drying and lyophilization; the microspheres having particle size ranging from 100 nm to 5 microns (abstract; column 8, lines 53-68; Example 1). Mathiowitz does not disclose the exact process steps. However, selection of any order of performing process steps is prima facie obvious in the absence new or unexpected results. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the microspheres according to Mathiowitz and modify the process as desired with the expectation of producing porous microsphere.

Khan: Khan discloses preparing ACTH containing microspheres by spray drying or evaporation of the solvent from emulsion containing pore forming agent; the particles have sizes ranging from 2-10 micron (abstract; column 7, lines 26-33; column 8, line 12). Khan does not disclose the exact process steps. However, selection of any order of performing process steps is prima facie obvious in the absence new or unexpected results. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the microspheres according to Khan and modify the process as desired with the expectation of producing porous microsphere.



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6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bernstein et al. (US 5,611,344) discloses porous microparticles prepared by solvent evaporation or spray drying (columns 7 and 8).

### ***Double Patenting***

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 16-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 11-14 of U.S. Patent No. 6,932,983. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of the issued claims used the composition prepared as per the method of the examine claims, the particle size, the TAP density and surface area in both the examined claims and the issued claims are the same.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara  
Patent Examiner  
Tech. Center 1600

A handwritten signature in black ink, appearing to read 'B. Fubara', is written over the printed name 'Blessing Fubara'.